

MEMORIAL HOSPITAL ISSUE

DELAWARE STATE MEDICAL JOURNAL

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VOLUME 29

APRIL, 1957

NUMBER 4

THE G.P. CAN TREAT PRURITUS ANI
LOCALIZED BRONCHIECTASIS IS CURABLE

Complete Contents on Page iv

relief
for your
patients

who develop nasal congestion
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REFERENCES

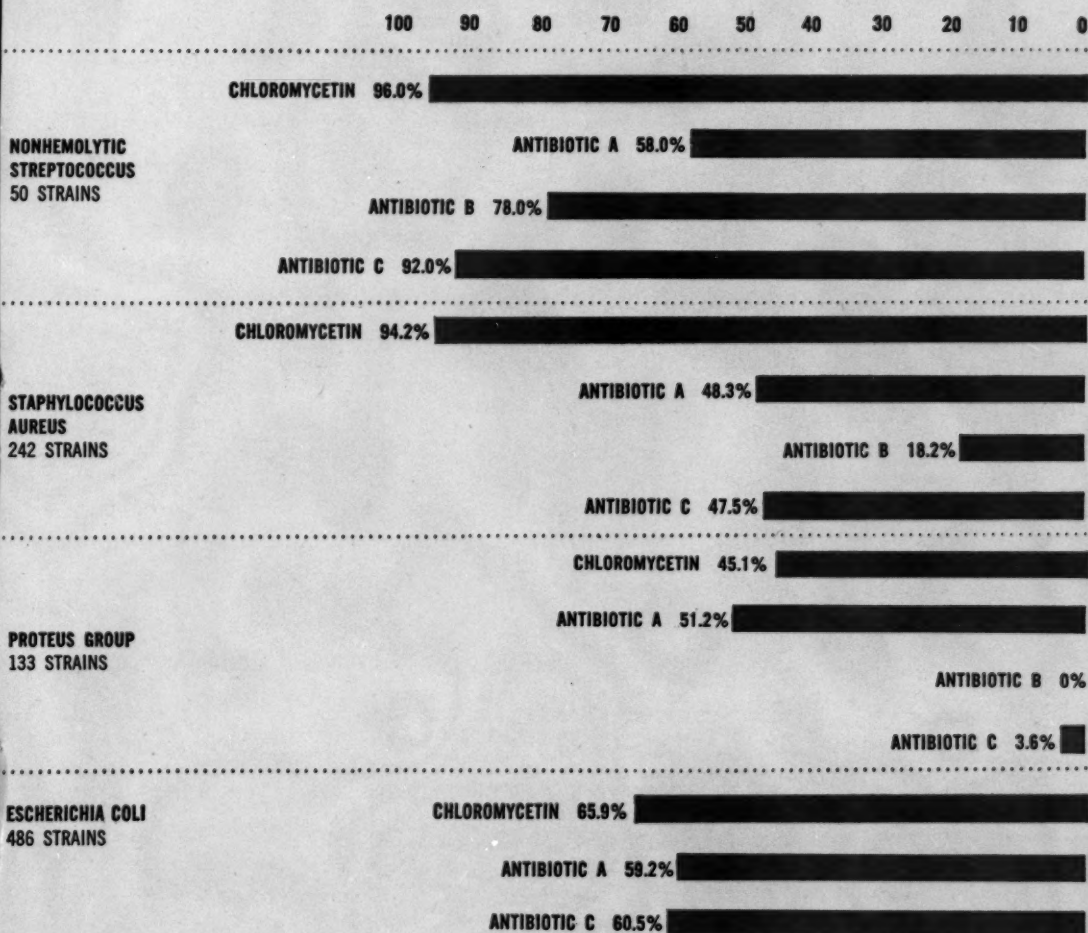
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This graph is adapted from Rantz and Rantz. It is based on *in vitro* studies of bacteria freshly isolated from clinical materials.

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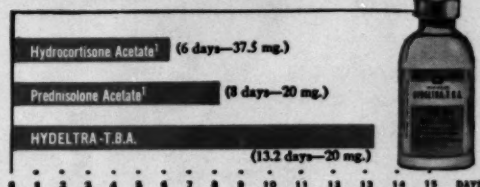
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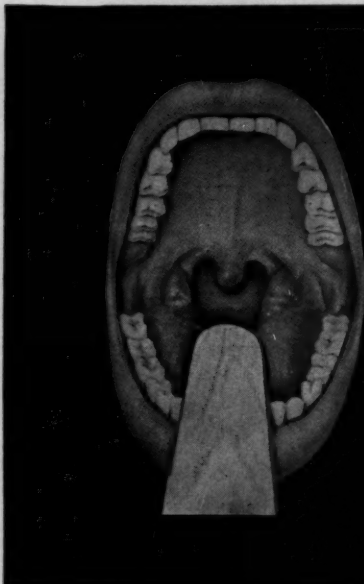
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1. Carter, C. H., and Maley, M. C.: Antibiotics Annual 1956-1957, New York, Medical Encyclopedia, Inc., 1957, p. 51.

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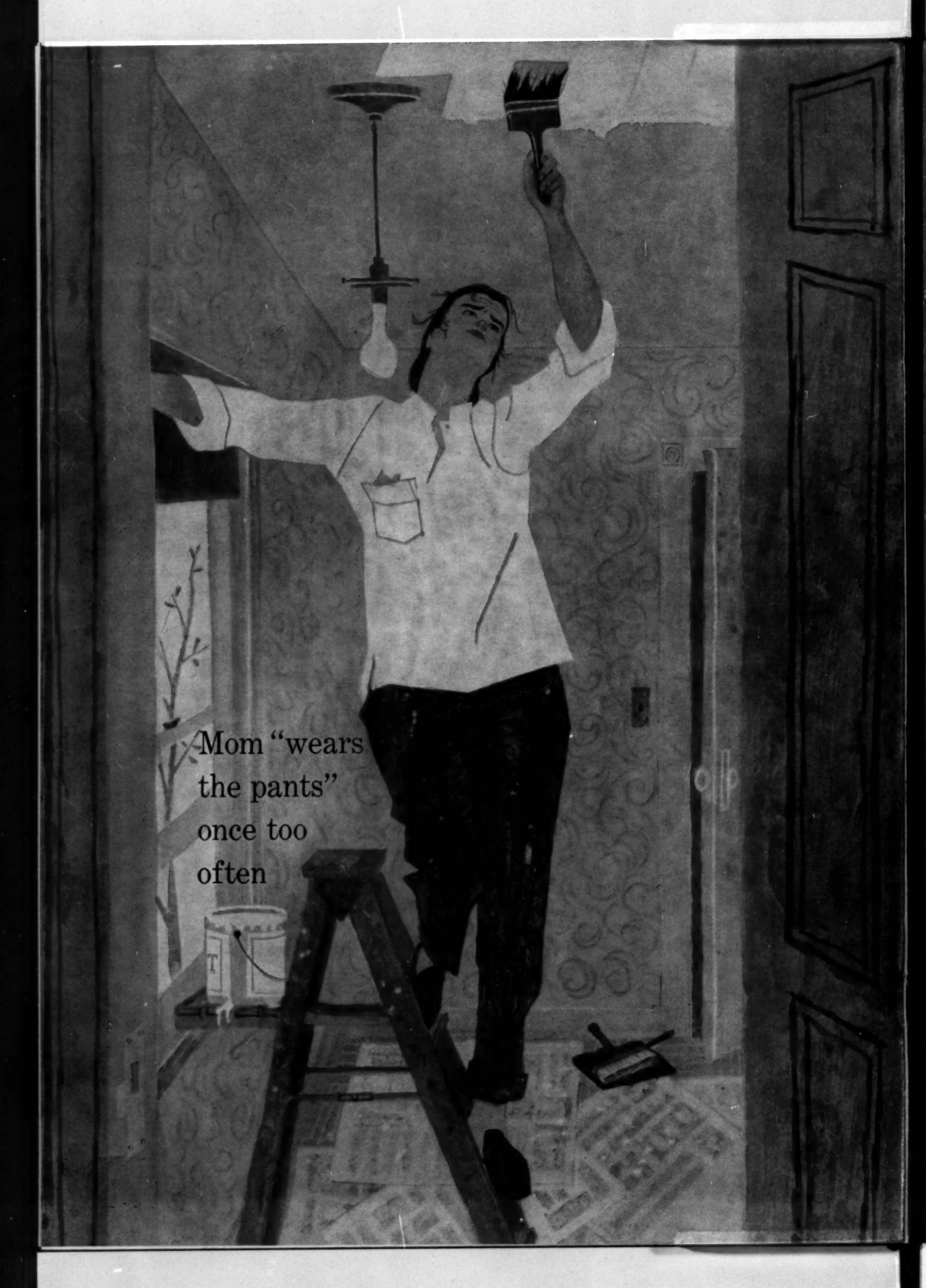
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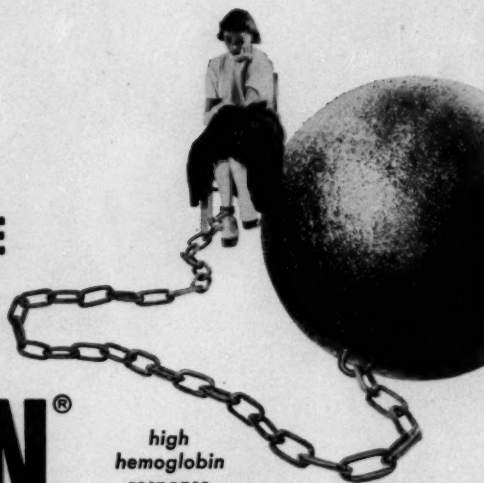
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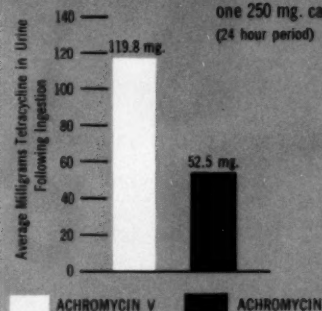
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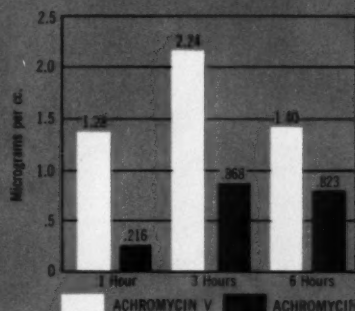
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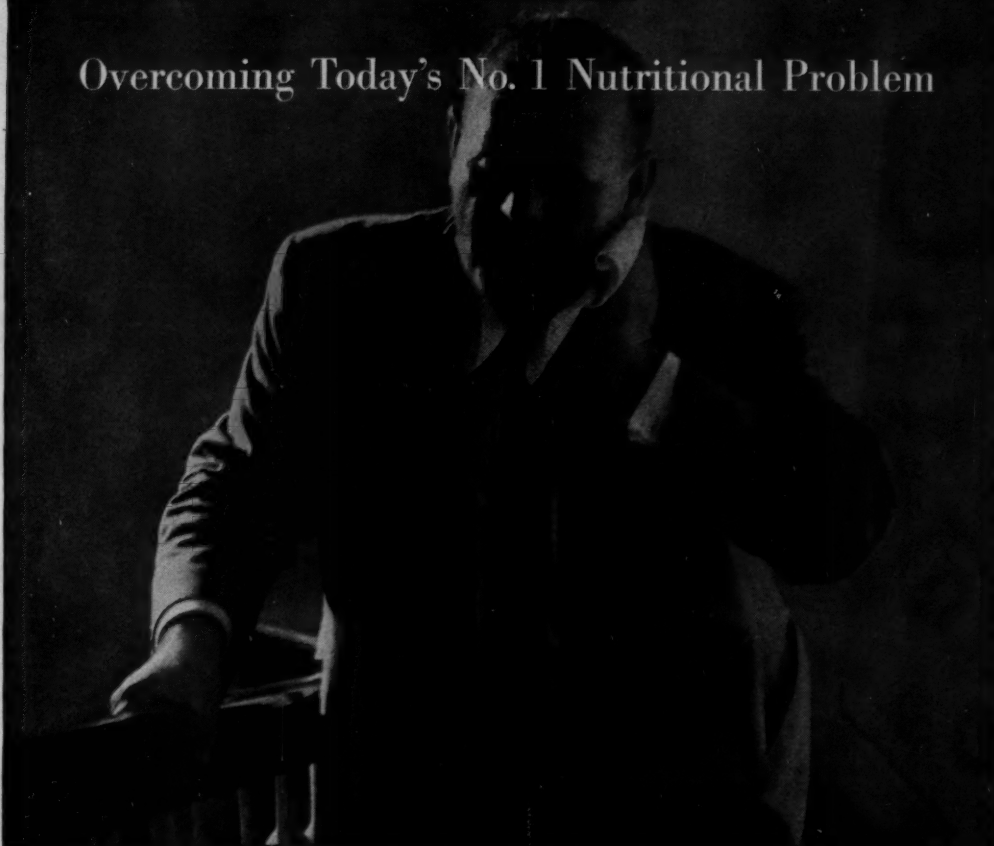
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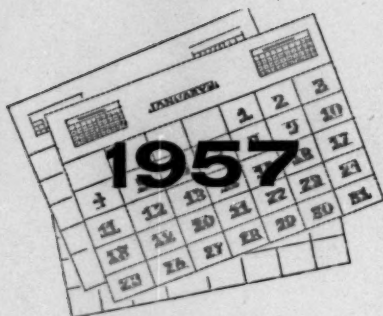
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MANAGEMENT OF PRURITUS ANI*

CALEB SMITH, M.D.**

This paper attempts to establish a practical approach to the treatment of pruritus ani that may be of value to the general practitioner. It is not a comprehensive review of the subject, and only those theoretical aspects that bear directly on treatment will be considered.

Pruritus ani is a symptom, not a disease. Its treatment is best approached through a somewhat empirical classification of its etiology, as follows:

1. NEUROGENIC PRURITUS ANI.

The cause of this type of pruritus ani is thought to be emotional stress. Often the stress is not considerable, but the patient's nervous system is a sensitive one. Unhappily, this type of pruritus ani accounts for at least 45% of the cases. Some observers place the figure as high as 70%.

2. PRURITUS ANI SECONDARY TO SURGICAL CONDITIONS OF THE ANORECTAL AREA.

This group comprises about 25% of the cases. Any anorectal lesion which tends to increase moisture locally, and hence promote maceration, is apt to cause pruritus. The following lesions are common offenders: Fissures, fistulas, draining sinuses, ulcers, mucosal prolapse, papillitis, cryptitis, skin tags, hemorrhoids, and neoplasms.

3. PRURITIS ANI SECONDARY TO DERMATOLOGICAL LESIONS.

This group accounts for about 20% of the cases. The following conditions are commonly implicated: Psoarasis, lichen sclerosis, syphilis, and dermatitis of the seborrheic, bacterial, mycotic or contact types.

4. PRURITIS ANI SECONDARY TO GENERAL CONDITIONS.

This group accounts for about 10% of the cases. The following states are commonly associated with pruritus ani: Diabetes, liver diseases, parasitic infestations of the intestinal tract (particularly pinworms), lymphomas, untoward reactions to antibiotics, genitourinary diseases (especially prostatitis and diseases associated with a vaginal discharge), any condition that causes chronic soft stools, poor hygiene, and allergy to hygienic pads, deodorants, foods, and the so-called -caine drugs.

Before treating pruritus ani, a serious effort should be made to establish a definite cause for the itching by means of a careful history, examination, and laboratory studies. If a diagnosis of secondary pruritus ani can be made, specific therapy may be available. Two practical points should be made, however. Pruritus ani resembles causalgia in that the longer it persists, the more difficult it is to relieve. It is almost impossible to relieve severe pruritus ani that has been present for more than two years. Therefore, patients with secondary pruritus ani should receive prompt treatment. Also, more than an occasional patient has secondary pruritus ani with a neurogenic element in it. For example, the patient with neurogenic pruritus ani and an annoying perianal skin tag may not be relieved by removal of the skin tag alone; he will also need treatment for his neurogenic pruritus ani.

It is the patient with neurogenic pruritus ani who presents the difficult problem. However, most of these patients will get satisfactory relief if they are treated intelligently and diligently.

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When the diagnosis of neurogenic pruritus ani has been established by exclusion (with experience one develops a high index of suspicion for neurogenic pruritus ani, but cannot depend on his hunch completely), the first step is to discuss the condition with the patient and give him an insight into his pruritus. Once this has been accomplished, the patient becomes much more tractable. A discussion of stress and sensitive nervous systems is beyond the scope of this paper, but a few practical points are worth mentioning. A patient should be made to realize that because he has a sensitive nervous system he is not necessarily inferior. Many of the people who have contributed greatly to the welfare of the world have had such nervous systems. Darwin, for example, was said to have such a sensitive nervous system that he was unable to have guests for dinner without being disabled the following day with diarrhea. Also, the patient should be given to understand that although there is always the possibility of the itching recurring, the longer he can keep it relieved by faithful treatment, the less apt it is to recur.

The next step is to help the patient understand pathological itching. Itching is a modified pain sensation. Physiologic itching travels over epicritic pain pathways, and is not an unpleasant sensation compared to pathologic itching. The latter travels over protopathic pathways, and is characterized by a burning, persistent, poorly localized, very unpleasant sensation. A patient with pathologic itching has a strong and natural desire to scratch. He must understand that when he scratches he does not relieve his pathologic itching, but merely replaces it in his sensorium with the less unpleasant epicritic pain, or itching. After scratching there is always a heavy discharge of impulses over the protopathic pathways, and the pathologic itching is aggravated. *Scratching perpetuates pathologic itching, and little can be done for the patient who will not give up scratching.* Fortunately, there is an easy method of relieving severe itching temporarily: cold water applied to the pruritic area will bring relief without later aggravating the itching.

Heat in any form, it should be noted, decreases the threshold to pathologic itching and should be avoided. One patient was considerably relieved by shutting off the heater beneath the seat of his automobile. It is worth emphasizing that the patient who has given up scratching has made one big step toward the permanent relief of his pruritus ani.

Good hygiene is the next step. The patient with pruritus ani must keep his perineum scrupulously clean, and he must be given explicit instructions about perianal hygiene. The usual procedure in using toilet tissue is to use a rubbing motion. Once the patient with pruritus ani starts this motion, he is bound to lose control of himself and rub vigorously; the result is scratching. The patient with pruritus ani must use a soft toilet tissue and "pat" himself clean. The first tissues should be dry; the next one or two should be wet with cold water; and subsequent tissues should be dry. Ordinary soaps should be avoided because alkalinity lowers the threshold to itching. The patient should be advised to use cool water and a surgical preparation containing hexachlorophene 3%, with a pH the same as that of the skin. Thorough cleansing should be done each night, and, if practicable, after each bowel movement.

Simple as the foregoing care is, it is the foundation for the successful treatment of pruritus ani.

Now for what should be "put on". The patient with longstanding pruritus ani has used so many preparations locally that one is apt to get a better result by stopping all medication than by prescribing one more ointment. Also there are several things that should not be used. The anesthetic ointments of the -caine type and antihistaminic ointments should be avoided as they commonly cause a sensitivity reaction which aggravates the itching. At the moment the market seems flooded with new anesthetic ointments that are said to cause little sensitivity. I rarely use them. Among the more effective preparations for local application are the following: (1) a lotion of ethyl alcohol containing 1% salicylic acid and 1% camphor, and (2) an oint-

ment composed of menthol 0.2 gm., phenol 0.3 gm., salicylic acid 1.0 gm., benzoic acid 2.0 gm., and Acid Mantle Creme (Dome) 60.0 gm.

Both these preparations are used on an empirical basis while the patient is learning to help himself, although both are reasonably effective against fungus infection, which is common. They should be applied each morning and evening after washing with the soap-substitute. The patient should be warned to use them sparingly because they cause a sharp burning sensation. After a few days, desquamation and relief of itching usually occur, and the patient suffers less burning when they are applied.

Patients with pruritus ani usually appreciate a sedative. Barbiturates are proscribed because they are apt to aggravate itching. Chloral hydrate or one of the tranquilizers are effective drugs.

The patient who does not respond to these simple measures within a month is a candidate for more active therapy. Steroids locally should be tried next. An ointment or cream containing Hydrocortisone Acetate 0.5% and Neomycin Sulfate 0.5% is one of a number of satisfactory preparations. Here again, explicit directions are necessary to obtain a good result. The ointment should be applied twice daily after cleansing the perianal skin with the soap-substitute and cool water. A small amount of the ointment, about the size of a pea, is sufficient for one application. The ointment should be rubbed in thoroughly but not vigorously. It is important not to discontinue the ointment abruptly, or recurrence is almost a certainty. Above all, the simple measures described previously should not be neglected. Many of the failures following the use of steroid ointments are due to their improper use and to neglecting of the general measures.

In extremely intractable cases steroids systematically should be tried. Here again, general measures should not be neglected and the steroid should be withdrawn gradually.

Finally, a few words can be said profitably about some of the methods of treatment that have limited usefulness. Tattooing of the perianal skin has been almost completely abandoned. Surgical operations designed to undercut the perianal skin and divide the subcutaneous nerves are rarely indicated; usually relief is obtained for about nine months, followed by a recurrence that is harder to treat than the original lesion because of the atrophy of the undercut skin. X-ray treatment gives excellent temporary relief, but here too recurrence with atrophic skin is so common that it has been largely abandoned. Alcohol injections under the perianal skin are used by a few proctologists; this method does have merit in selected cases, but a meticulous technique must be followed to get a good result and avoid troublesome complications. Sympathectomy has been used in a few severe cases with promising results. Psychiatric treatment has brought relief to some patients when all else has failed.

SUMMARY

Accurate etiologic diagnosis is essential for the proper treatment of pruritus ani. If it is secondary to surgical, dermatological or general conditions, removal of the primary condition may be possible. Forty-five to 70% of the cases, however, are primary or neurogenic. Little can be done for the patient who will not give up scratching. A regimen has been outlined, however, that frequently is successful in the cooperative patient.

LOCALIZED BRONCHIECTASIS IN THE ADULT PATIENT*

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LORING E. SYLVESTER, M.D.***

Localized bronchiectasis in the adult is a commonly encountered disease on a Thoracic Surgical Service. It is, however, frequently unrecognized since hemoptysis and recurrent upper respiratory infections may be the only symptoms. Because localized bronchiectasis often does not cast a shadow or displace the pulmonary contents on the chest x-ray, the diagnosis may remain obscure. Treatment with antibiotics may cause a prompt subsidence of the febrile episodes and further serve to hide the underlying pathologic process. Bronchoscopic examination in these cases is usually noncontributory except as an aid in determining the site of hemorrhage. Bronchography of all the bronchial segments is essential to make an accurate diagnosis and to plan therapy. In contrast to the multicentric bronchiectasis seen in children, the adult localized form readily lends itself to surgical resection and has an excellent prognosis.

We have observed this process in six patients in the last two years, all of whom have undergone surgical resection with pathologic examination of the diseased lung tissue. All of these patients first consulted a physician because of hemoptysis; five of them had recurrent bouts of hemorrhage. It is of interest that the routine antero-posterior and lateral chest x-rays were comparatively normal in five cases. The sixth patient had minimal roentgenographic changes in the lingula of the left lung. Bronchoscopic examination revealed normal findings in three of our patients. One showed bleeding from the left lower

lobe, one purulent secretions from the left lower lobe, and one had granulation tissue in the right lower lobe. The diagnosis of localized bronchiectasis was not established prior to bronchography in any of the cases.

Reports of four illustrative cases follow:

Case No. 1: A 41 year old white man was admitted to the hospital because of recurrent hemoptysis with a productive cough. He gave a history of pneumonia in August 1955 with fever, cough and pain in the left lower chest. He was studied at that time in another institution where bronchoscopy was negative and the routine antero-posterior and lateral x-rays of the chest were read as being completely normal. He was finally discharged from the hospital with a diagnosis of bleeding from the pharynx. He was admitted to the Memorial Hospital in January 1956 having had several more bouts of hemoptysis, varying in amount from a teaspoon to half a cup. Physical examination was entirely negative, bronchoscopy was normal, but a bronchogram showed bronchiectasis of the basilar segments of the left lower lobe. Massive pleural adhesions about the left lower lobe were found at operation and a left lower lobectomy was performed. The pathologic examination revealed a sacculated bronchiectasis of all the basilar segments. The patient was discharged from the hospital eleven days after admission and has resumed his normal activities.

Case No. 2: A 35 year old white woman was admitted to the hospital because of recurrent bouts of hemoptysis over a six year period. Her first bout of hemoptysis was in 1950, approximately three months after a tonsillectomy. She had repeated severe episodes of bleeding; these increased in

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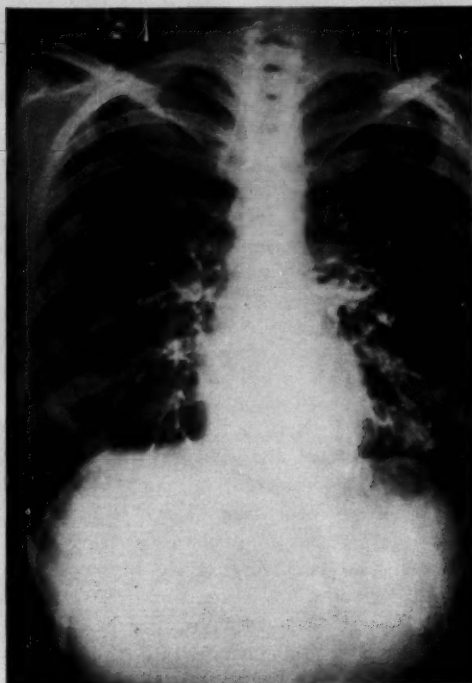


FIGURE 1—Bronchogram of patient No. 2 showing severe saccular bronchiectasis of the superior segment of the left lower lobe.

frequency. At times she would cough up as much as a pint of blood. She remained asymptomatic between attacks of hemorrhage. She was studied in another city where bronchoscopy and routine chest x-rays showed no abnormality and she was discharged without a definite diagnosis. On admission to the Memorial Hospital, although bronchoscopic findings were comparatively normal, a bronchogram revealed severe saccular bronchiectasis in the superior segment of the left lower lobe. (Figure 1.) The patient had a left lower lobectomy and was discharged from the hospital eight days following surgery. She has resumed her occupation of running a small bakery and has remained asymptomatic to date.

Case No. 3: A 53 year old white woman was admitted to the hospital on September 7, 1955 complaining of repeated episodes of hemoptysis, recurrent upper respiratory infection and large amounts of purulent sputum. The hemoptysis occurred after she had pneumonia in 1938, and after recurrent

bouts in 1940 and 1954. Physical examination was normal on admission; her chest x-ray was entirely normal but a bronchogram done on September 12, 1955 showed a lack of filling of the distal lingular bronchi. On September 27th a right bronchogram was negative. She then underwent, without incident, a segmental resection of the lingula on the left side; pathologic examination revealed severe bronchiectatic cylindrical and saccular change in the lingular bronchi of the left upper lobe. The patient was discharged from the hospital nine days after surgery and has had no postoperative complications. She resumed her duties as a housewife and has remained asymptomatic.

Case No. 4: A 28 year old white man was admitted to the hospital with a history of weakness, malaise, a cough productive of foul smelling sputum, recurrent febrile episodes and occasional hemoptysis. These complaints had been present for two years. He had developed clubbing of the nails six months previous to admission and had been

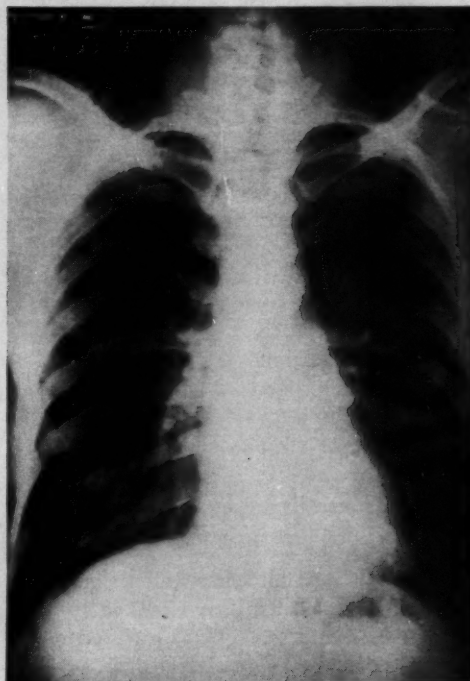


FIGURE 2—Patient No. 4—routine chest x-ray showing no abnormalities of significance.

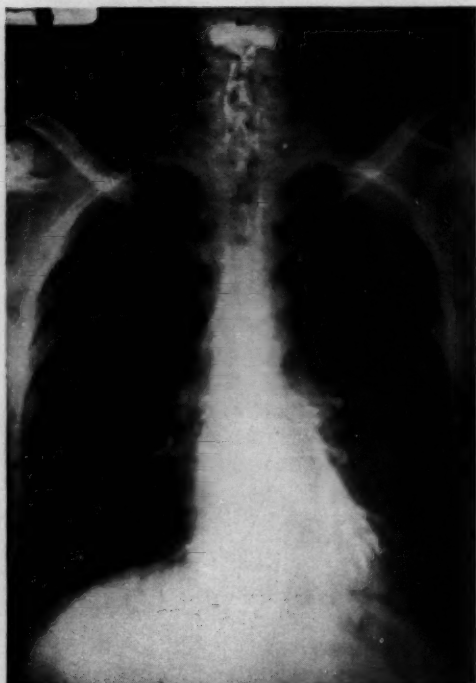


FIGURE 3—Patient No. 4—bronchogram showing bronchiectasis of basilar segment of left lower lobe.

studied elsewhere at which time bronchoscopy and bronchography had demonstrated bronchiectasis. Conservative management failed. A chest x-ray (Figure 2) was negative but bronchoscopy and a bilateral bronchogram (Figure 3) revealed bronchiectasis in the left lower lobe. At operation, massive adhesions were found about the left lower lobe which presented infiltration and thickening of all its basilar segments as well as marked hilar lymphadenopathy. Pathologic examination confirmed the presence of bronchiectasis involving all the basilar segments. His post-operative recovery was uneventful.

PATHOGENESIS OF LOCALIZED BRONCHIECTASIS

Although inflammation and its sequelae are the basic mechanisms for the production of bronchiectasis, be it diffused or localized, there are ancillary factors which in any given case may limit its inception and progression to a localized area. Certainly, foreign body aspiration with pro-

longed retention is such a factor and the history of such an episode strengthens one's confidence in the findings of localized disease on bronchography and permits an optimistic outlook following surgery. With this mechanism, the resulting lung abscess may blend with bronchiectasis. Other conditions such as compression by lymph nodes or tumor, broncholiths and broncho stenosis which produce partial or complete obstruction of the smaller bronchi will give the same result.¹

On the other hand a relatively diffuse process recorded clinically as "pneumonia" or "influenza" may yet leave its mark only on a portion of the affected area. This is due to local necrosis or failure of resolution and lack of reeration of the lung tissue. Multiple cavities may coalesce, their walls epithelialize, and surrounding inflammation subside leaving few clues as to the original event. Poor local drainage, fibrosis and unaerated lung may perpetuate the inflammatory process. Granulation-lined cavities with their abundant secretions may themselves interfere with drainage and infect adjacent tissue and thus the process spreads by contiguity.

The predilection of bronchiectasis for the lingula, right middle lobe and basal segments of the lower lobes is mute evidence of the effect of gravity and the importance of drainage. Again, their effect tends to restrict the process to the immediate bronchopulmonary system. Of our six patients, four had involvement of the left lower lobe and one each the right lower and left upper lobes.

Whether developmental factors play their part in localized bronchiectasis is conjectural although Schwartz and Katz¹ suggest this may be true. Certainly it may be difficult to differentiate in some cases between congenital bronchogenic cysts and markedly dilated thin walled bronchiectatic cavities when the tell-tale inflammation has subsided.

DISCUSSION

Since Laennec first described bronchiectasis in 1819 and Sicard and Forestier introduced the endobronchial iodized oil

bronchogram in 1922, the clinical opinion regarding bronchiectasis has undergone waves of enthusiasm for surgical resection. Many authors have differentiated between childhood bronchiectasis, with its progressive inexorable course, and that occurring in the adult which tends to remain localized for years. At the Mayo Clinic, Cooley, et al², stressed that surgical results were much poorer in children, with 16.6% of surgically resected cases developing new bronchiectasis. In their series of cases followed five years only 60% could be credited with receiving a good result. In contrast, Ginsberg³, in reviewing all the cases, regardless of age, at the Mayo Clinic, showed 76% good results following surgical extirpation. He stressed the fact that residual disease after surgery is the most significant factor affecting the prognosis. Lindskog⁴ gave an excellent summary of the criteria for surgery: 1) Symptoms severe enough to cause discomfort, inconvenience and complications. 2) Proven and localized bronchiectatic changes by bronchography. 3) An adequate cardiorespiratory reserve and 4) No contraindications from concurrent disease. Meade's⁵ series from the Kennedy General Hospital demonstrates how low the surgical mortality rate may be. (0.5%)

Three of our patients were previously hospitalized at other institutions and discharged without the diagnosis of bronchiectasis being made because routine chest x-rays and bronchoscopy were normal. All of the patients were healthy adults, the youngest being 22 and the oldest 53 years of age. Four lobectomies and two segmental resections were performed without incident and there were no postoperative complications. The patients have been followed six to twenty-four months and all have resumed their former duties with no signs or

symptoms of residual disease. There has been no incidence of postoperative hemoptysis, pneumonitis, or abnormal sputum production.

SUMMARY

Bronchiectasis which has remained confined to a lobe or segment of a lobe is a disease which may be attacked surgically with a confident expectation of a complete cure. Hemoptysis, increased purulent sputum and recurrent upper respiratory infection should always suggest the possibility of bronchiectasis. Bronchoscopy and routine chest films are inadequate tools with which to rule out this condition. Bronchography is necessary to confirm the diagnosis and accurate mapping of all bronchial segments is essential to plan the surgical resection.

CONCLUSIONS

1. Adult localized bronchiectasis in contrast to the childhood type has an excellent prognosis if surgical resection is utilized.
2. Hemoptysis, recurrent upper respiratory infection and abnormal amounts of purulent sputa are the symptoms most frequently found.
3. Bronchography is necessary to make a diagnosis of localized bronchiectasis.

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EARLY PRIMARY PERITONEAL PREGNANCY*

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Ectopic pregnancy has been a frequently discussed subject. Since January 1954, 447 articles have appeared in the literature dealing with all phases of extrauterine pregnancy. Primary peritoneal pregnancy is a rare entity and the literature contains only a few articles on the subject.

The validity of the concept of primary peritoneal nidation is difficult to prove. Most abdominal pregnancies have been attached to the uterus, ovaries, or Fallopian tubes, and have been considered tubal abortions with secondary peritoneal attachment. Advanced abdominal pregnancies have been reported in which attachment has occurred at a distance from the pelvic organs, but these have been difficult to authenticate as being primary. Many have theorized that the fertilized ovum will attach only to tissue of Müllerian origin.

Studdiford¹, in 1942, reported a case of abdominal pregnancy in which, although placental attachment had occurred on the posterior surface of the uterus, no connection with the endometrial cavity could be found. The gestational age was estimated at four weeks, making secondary implantation highly improbable. He advanced the following criteria for proof of primary peritoneal pregnancy:

- 1) That both tubes and ovaries are normal with no evidence of recent or remote injury,
- 2) the absence of any evidence of uteroperitoneal fistula, and
- 3) the presence of a pregnancy exclusively related to the peritoneal surface, and young enough to eliminate the possibility of secondary implantation following a primary nidation in the tube.

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Best² had stated essentially the same criteria in 1931, with the exception of the gestational time element, but not until the report of Studdiford's case was the concept of nidation of the blastocyst upon the peritoneum accepted.^{3,4}

Abdominal pregnancy of any type is unusual. Beacham⁵ states that it occurs in white females once in 11,419 live births, and once in 685 live births in the Negro race. Douglass and Kohn,⁶ however, say that it occurs much less frequently; once in 67,534 births in the white race, and once in 4,188 births in the Negro race. Ahnquist and Lund⁷ list only ten cases of primary peritoneal pregnancy in their comprehensive presentation of the subject.

CASE REPORT

An eighteen year old white woman was admitted to the surgical service at the Memorial Hospital on March 12, 1957, after being seen in the Emergency Ward. She had been in perfect health until 36 hours prior to admission, at which time she noted crampy lower abdominal pain, more severe on the left. Moderate difficulty in walking was associated with the pain. The patient denied shoulder-top pain. There had been no gastro-intestinal disorder, fever, urinary complaint, or vaginal discharge or bleeding. The last normal menstrual period had occurred January 29th. The last menstrual period had begun February 26th but had lasted only two instead of the usual five days. This had been attributed to fatigue associated with a long automobile trip. The systemic review was non-revealing. The previous history included one normal pregnancy.

The family physician was called about 12 hours after the onset of the illness. He found the pulse to be 140 per minute, but his examination revealed no other positive

findings. At this time members of the family thought that she was very pale.

The crampy pains continued and became progressively severe. They were accompanied by nausea and finally, vomiting. The family physician found a tachycardia of 160 per minute and a systolic blood pressure of 70 mm Hg. A marked increase in pallor was noted. The patient was sent to the hospital.

On examination, the patient was extremely pale but was in no acute distress. The pulse was 140-156 per minute and although regular, was greatly decreased in volume. The blood pressure was 90/40. The temperature was recorded at 100.6°F. The positive physical findings were limited to the abdomen which was slightly full. Striae gravidarum were present. There was pain localized in the left supra-pubic area. This was aggravated by deep inspiration and cough. There was generalized muscle guarding in the lower abdomen, with rebound tenderness in the left lower quadrant. Peristalsis was present. The tentative diagnosis of ectopic pregnancy with intra-peritoneal hemorrhage was made, and because of the danger of causing further bleeding, a pelvic examination was not done. A rectal examination revealed a slightly tender mass of spongy consistency and indeterminate size occupying the cul-de-sac.

Intravenous Dextran was started immediately as an emergency blood volume expander, and preparations were made for laparotomy. Laboratory studies revealed the hemoglobin to be 7.2 Gm. /100 ml., rbc 2.78 million/ccm, and the hematocrit 24.4%. The wbc was 36,950, segmented forms 78%, non-segmented forms 14%, and lymphocytes 8%. Urinalysis was normal except for 100 rbc/hpf and a trace of albumin. Transfusion with whole blood was begun immediately prior to surgery.

The patient was given endotracheal cyclopropane-ether anesthesia with succinylcholine chloride. The abdomen was quickly opened through a lower midline vertical incision. As the peritoneal cavity was opened, revealing 1500-2000 cc of liquid and clotted blood, the pelvic organs were immediately

elevated into the wound for inspection. The uterus, ovaries, and tubes were found to contain no evidence of ectopic or intrauterine pregnancy. After aspiration of blood from the pelvis, a mass of clotted blood and tissue was removed from the cul-de-sac. The bleeding point was then located on the left postero-lateral peritoneum of the cul-de-sac, where there was a 2.5 cm. diameter plaque of brownish-red friable tissue adherent to the peritoneum. Attempts were made to control the bleeding with hot moist packs. The removed tissue mass was then closely inspected and found to consist of blood clot, placental tissue, and a fetus contained in an intact amniotic sac. The bleeding point was again inspected, and because the bleeding could not be controlled, the area was excised. After reperitonealization, the operative field was dry. Prior to closure of the wound, the Fallopian tubes were again closely inspected, but no evidence of a pre-existing tubal pregnancy could be found.

The fetus measured 3.2 cm, in total length, an estimated gestational age of six or seven weeks. Histologic examination of the excised peritoneum revealed adherent placental tissue. A post-operative Friedman test was positive.

The post-operative course was uneventful. The pulse rate returned to normal after transfusion of 2000cc whole blood. The patient was discharged from the hospital on the sixth post-operative day.

SUMMARY

A short summary of the literature concerning primary peritoneal pregnancy is presented with a case report of what we believe to be an undisputable instance of primary peritoneal nidation in that it satisfies the criteria set forth by Studdiford.

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ASEPTIC NECROSIS OF THE FEMORAL HEAD DUE TO SICKLE CELL - THALASSEMIA DISEASE*

CASE REPORT

C. S. PAPASTAVROS, M.D.**

Differentiation of sickle cell anemia and sickle cell trait associated with anemia due to other causes was, until recently, difficult or even impossible. Accurate diagnosis is important since sickle trait is a benign disease while sickle cell anemia runs a more stormy course with hemolytic anemia, "crises", jaundice, and early death.¹³

It has been shown^{9,13} that the red cells of individuals with sickle cell trait contain normal and sickle hemoglobin, while the ones from patients with sickle cell anemia contain only abnormal hemoglobin. The type of hemoglobin present is easily differentiated by electrophoresis.

Reich and Rosenberg¹² reported three cases of aseptic necrosis of bone in Caucasians with chronic hemolytic anemia due to combined sickling and thalassemia traits. They are the only reported cases, to our knowledge, presenting bony changes. Several authors (Powell, Rodarte, Neel) have reported a total of fifteen cases of sickle cell-thalassemia disease without definite evidence of aseptic necrosis of bone.

Smith and Conley¹³ reported four cases of sickle cell-thalassemia and 16 cases of sickle cell anemia hemoglobin C disease. Four of their patients showed osteochondritis of the femoral head apparently due to aseptic necrosis. They stressed the fact that none of their patients with sickle cell anemia showed aseptic necrosis of bone. Tanaka et al¹⁴ reported six patients with sickle cell anemia (homozygous S), proven by electrophoresis, who had aseptic necrosis of the femoral head.

CASE REPORT

The patient, a thirty-eight year old white man of Greek descent, entered the hospital with the chief complaint of pain in his right hip. He had a long history of difficulty with his back and lower extremities. His hip pain had been persistent for one year. X-rays done prior to admission were reported to reveal some bone disease in the region of the right hip and he was admitted for examination by biopsy.

He had a history of splenectomy when he was 13 years old for anemia. Full details were not available.

Physical examination was not remarkable except for some limitation of abduction of the humerus bilaterally, loss of motion of the right thigh, and tenderness to palpation over the right hip area.

There were 4.9 million red blood cells with 13.1 Gm. hemoglobin. There were 14 nucleated red blood cells per hundred white blood cells. Pathological report of the biopsy from the right femoral neck showed granulation tissue with no bony pathology. The patient was discharged from the hospital.

Six months later he had 4.6 million red blood cells with 13.6 Gm. hemoglobin and 11 nucleated red cells per hundred white blood cells. His white cell count was 15,500. The stained smear showed one metamyelocyte, many target cells, 2+ stippling, 3+ achromia and strongly positive sickling with sodium bisulfate.

The electrophoretic pattern was run on several occasions and it was the final conclusion that in addition to the very prominent amount of sickle hemoglobin there

* From the Department of Roentgenology, Memorial Hospital.

** Papastavros, Christos, M.D., Graduate Fellow in Roentgenology.

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FIG. 1—Aseptic necrosis of the right femoral head. Loss of normal rotundity of the head with evidence of sequestrum formation and sclerosis of the bone.

was evidence of a small amount of normal A hemoglobin representing perhaps 10 or 15% of the total. Fetal hemoglobin determination showed a value slightly over 5.5% which is distinctly abnormal.

X-ray findings eight months prior to admission showed an osteoblastic reaction in the head of the right femur. Later films showed the osteoblastic activity, with areas of decreased density interspersed between these thickened areas. Films taken one year after the initial studies showed evidence of loss of the normal rotundity and smoothness of the right femoral head indicating a necrotic type of involvement. This was thought to be aseptic necrosis associated with evidence of a depressed sequestrum and sclerotic adjacent bone (figure 1).

Re-examination sixteen months later revealed further destruction of the head of the right femur with fragmentation and flattening of the weight bearing portion of the femoral head and secondary hypertrophic arthritic changes about the joint



FIG. 2—Progressive changes with deformity and flattening of the head of the right femur.

(figure 2). Recent x-rays of the shoulders showed changes in the left shoulder similar to those found in the right femur.

DISCUSSION

Capillary thrombosis resulting in infarction^{7,12} of the involved bony area, presumably, is responsible for the aseptic necrosis in sickle anemia. Phemister^{10,11} described the changes in bones and joints resulting from interruption of circulation and postulated that changes in the density of the bone in necrosis may result from "atrophy of disuse, from creeping replacement of dead bone by new bone, from pathologic fractures, and collapse of the dead bone bordering on joints, from compression of dead trabeculae, from infiltration of bone sand into the dead marrow spaces, and from calcification of the line of demarcation and the interim of old stationary necrotic areas located in the medullary and cancellous regions".

Aseptic necrosis of bone in patients with

sickling phenomenon and sickle cell anemia (S-S) apparently occurs with varied frequency and cannot be used, as suggested, as differential of genetic variants of sickle cell phenomena and sickle cell anemia (S-S). Only electrophoresis permits the separation of sickle cell anemia from its genetic variants.

Roentgenographically, aseptic necrosis in sickle cell anemia should be differentiated from Caisson disease, Legg-Perthes disease, advanced hypertrophic arthritis, post-traumatic necrosis, slipped femoral epiphysis, and Gaucher's disease.

Aseptic necrosis of the head of the femur and sickle cell anemia (S-S) according to Tanaka et al¹⁴ occurs in approximately 12% of the patients and might be an incapacitating complication though it can occur in asymptomatic patients.

Since bony changes in the form of aseptic necrosis, involving as a rule the femoral heads and to a lesser degree the humeral heads, occur with varied frequency in both sickle cell anemia and its genetic variants, the radiologist is well justified to include the above diseases in his differential diagnosis in patients of certain race and age suffering with blood dyscrasia.

Aseptic necrosis of the femur or humerus is not the only bony change occurring in this group of patients.^{1,2,3,4,5,6,8,14}

This case apparently is the fourth to be reported of aseptic necrosis of the head of the femur and humerus in a patient with sickle cell-thalassemia disease.

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SEMI-ANNUAL MEETING DELAWARE VALLEY CHAPTER AMERICAN MEDICAL WRITERS' ASSOCIATION DATE: MONDAY, MAY 20, 1957

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PROGRAM

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Problems of a Medical Editor..... Col. John B. Coates, Jr., M.C., U.S.A.

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THE INCIDENCE AND SIGNIFICANCE OF ANTIBIOTIC-RESISTANT ORGANISMS IN HOSPITALS AND THE COMMUNITY

by

R. J. BISHOFF, M.D.

Dover, Delaware

Although increase in the incidence of antibiotic-resistant micro-organisms has been magnified by reports from hospital communities where infections due to resistant organisms have become a major challenge, out-patient and private patient treatment have not been affected greatly. However, unless precautionary measures are taken at the hospital level, the incidence of drug-resistant organisms may rise also in the community.^{1,2}

What is drug-resistance and how does it come about? Drug-resistance is the expression of a fundamental biological phenomenon and is best defined as *adaptation*.² By adapting themselves, organisms are able not only to live in the presence of an antibiotic previously deadly to them, but also to produce progeny that are unaffected by the drug. Several mechanisms have been suggested to account for the appearance of these drug-resistant strains of bacteria. According to Lepper,³ two mechanisms seem to be more important than the others: first, the ability of the organism to bypass the effect of the drug; and second, the ability of the organism to produce enzymes that inactivate the antibiotic.

The first mechanism takes into consideration naturally resistant bacteria and bacteria that become resistant through hereditary and non-hereditary changes in their metabolism while being exposed to an antibiotic. Observations concerning the second mechanism show that resistance attributable to the production of drug-inactivating enzymes is dependent on the speed with which the enzyme is produced, the

potency of the enzyme, the size of the bacterial population producing the enzyme, and the concentration of the antibiotic being used to combat the infection.^{4,5,6} The last two observations are important clinically in view of the tendency of some bacteria to become concentrated in tissues such as the lungs or endocardium. As the bacterial population becomes larger, the concentration of enzyme increases and larger doses of antibiotic must be used to overcome the inactivating effect of the enzyme. Other investigators^{2,7} conclude that no one mechanism is responsible for the appearance of drug-resistant bacteria, but that they emerge because of the combined effects of several mechanism operating independently.

Practically all bacteria possess the ability to develop some degree of drug resistance, but most organisms do not develop sufficient initial resistance to overcome bactericidal effect of an antibiotic and, therefore, rarely become resistant. However, some organisms develop resistance rapidly and are

TABLE I
PROPENSITY OF MICRO-ORGANISMS
TO DEVELOP RESISTANT STRAINS

Group	Micro-Organisms	Frequency of Appearance of Resistant Strains
1	Pneumococcus, Meningococcus, Beta hemolytic streptococci (excluding group D streptococci) Gonococcus, Shigella, Hemophilus influenzae	Seldom, if ever
2	Alpha and gamma streptococci Coliforms, Proteus, Pseudomonas, Micrococcus (Staphylococcus), Mycobacterium tuberculosis	Often
3	Brucella, Salmonella typhi, Rickettsia	Seldom, if ever

able to withstand the antibacterial effect of a drug even before a normal course of therapy is complete. Lepper³ divides organisms into three categories based on their ability to become resistant, (Table 1). Since the micrococci (staphylococci) are most frequently involved in infections that are refractory to antibiotic therapy, the remainder of this discussion will be limited to them.

ANTIBIOTIC-RESISTANT STAPHYLOCOCCI IN HOSPITALS

The appearance of antibiotic-resistant staphylococci in hospitals is unique because no other species of micro-organisms pose such a world-wide problem. In 1942, Rammelkamp and Maxon,⁸ working in this country, were among the first to report on the isolation of penicillin-resistant strains of staphylococci from hospitalized patients. Subsequent investigators showed that these strains of staphylococci were naturally resistant to penicillin because they produced an enzyme, penicillinase, which inactivated the drug.^{4,5} Reports from other parts of the world followed. Barber and her associates⁹ in England found that the incidence of penicillin-resistant staphylococci increased from 14.1% in 1946 to 59.0% in 1948. Rountree and Thomson¹⁰ at the Royal Prince Alfred Hospital in Sydney, Australia, showed that 59% of the 228 strains of staphylococci isolated from hospitalized patients during 1948 and 1949 were resistant to penicillin. In 1950, a report from Norway¹¹ gave the incidence of penicillin-resistant staphylococci isolated from patients before treatment with the drug as 15.5%. Following treatment with

penicillin, 68.1% of the organisms isolated from the same patients had become resistant. One of the most comprehensive reports on staphylococcal resistance issued in this country is that of Spink² (Table 2). It seems evident that drug-resistant strains of bacteria are appearing in hospitals with greater frequency than in the past.

Resistant strains of staphylococci may originate from a few naturally resistant organisms by selective passage through patients who have been treated with antibiotics. Once the resistant strain is established, its subsequent incidence depends on the frequency with which an antibiotic is used against it. Lepper, Dowling, Jackson and Moulton¹² clearly illustrated this by conducting an experiment in which the use of penicillin was discontinued in favor of erythromycin for five months. At the beginning of the experiment, 50% of the staphylococci isolated from patients and hospital personnel were penicillin-resistant; resistance to erythromycin was negligible. At the end of the test period, the incidence of penicillin-resistant staphylococci had dropped to 35%, while erythromycin resistance rose from 0.0% to 70.0%. During the 4 months following the experiment, the use of erythromycin was discontinued and penicillin was re-instituted. The incidence of resistant organisms to penicillin rose sharply from 35% to 80%, and erythromycin resistance dropped to 28%. As pointed out by Kempe,¹ it would be of considerable interest to know what might occur in the community if a similar experiment were performed.

Hospital dissemination of antibiotic-resistant staphylococci occurs directly from patient to patient to some extent. Intermediate carriers, however, have proved to be the most important vector in the transmission of these organisms. Studies have shown that resistant strains are carried on the skin and in the nasopharynx of physicians, nurses and other hospital personnel, and that the organisms frequently replace the normal nonpathogenic, non-resistant flora of patients being treated at the hospital. Kempe¹ uses the term "cross infection-replacement" to describe this phe-

TABLE 2
PERCENTAGE OF RESISTANT
STAPHYLOCOCCI ISOLATED
FROM HOSPITALIZED PATIENTS

	1942	1951	1952	1953
Penicillin	12.0	62.5	57.2	62.7
Streptomycin	—	48.0	48.8	65.3
Chloramphenicol	—	25.0	2.5	0.6
Oxytetracycline	—	38.0	47.5	62.7
Chlortetracycline	—	23.0	33.2	62.7
Erythromycin	—	—	0.0	18.3

TABLE 3
METHODS OF MINIMIZING ANTIBIOTIC
RESISTANT INFECTIONS

1. Combinations of drug
2. Introduction of new drugs
3. Gradual return of sensitive strains after a drug usage has been decreased
4. Reducing the use of all antibiotics to a minimum
5. Use of minimal effective dose and limited anti-bacterial spectrum
6. Careful bacteriologic studies before treating individuals with chronic infections and/or mixed infections
7. Treatment only for evidence of infection and not for presence of bacteria.
8. Remedy of underlying anatomic, immunologic or metabolic defect when possible
9. Nursing precautions to avoid interchange of organisms between personnel and patients

nomenon and implies that it is certain to have an impact on public health in general.

Since the appearance and dissemination of antibiotic-resistant staphylococci seems to be an easy and universal matter in hospitals, steps must be taken to reduce the incidence of these organisms and to keep them from spreading to private practice. Opinions of several authorities regarding steps that should be taken to prevent the spread of antibiotic-resistant strains of bacteria have been summarized by Lepper³ and appear in Table 3.

ANTIBIOTIC-RESISTANT STAPHYLOCOCCI IN THE COMMUNITY

There is considerably less information in the literature regarding the incidence of antibiotic-resistant staphylococci in the community than there is for the incidence of such organisms in hospitals. This lack of information results from an effort to spare the patient the inconvenience and cost of bacteriological tests. Also, in private practice, it is usually necessary to initiate immediate therapy when first seeing an acutely ill patient.

Prior to 1949, there is little or no mention in the literature of the incidence of antibiotic-resistant organisms in the community. In 1949, Martin¹³ found that 20% of the staphylococci isolated from healthy adults were resistant to penicillin. Sum-

mers¹⁴ reported that 43% of the coagulase positive strains of staphylococci isolated during 1952 at an ear, nose, and throat out-patient clinic were penicillin-resistant. Fusillo¹⁵ and Oswald,¹⁶ reporting separately, found the incidence of penicillin-resistant staphylococci for overlapping periods during 1953 and 1954 in and around Washington, D. C. to be 17.8% and 17.5% respectively. The former report also gives the incidence of chlortetracycline and oxytetracycline-resistant organisms to be less than 5%. A study which indicates what can be expected before resistance to a drug is built up was conducted recently in Dover, Delaware.¹⁷ Of all staphylococci isolated from patients, only 2% were resistant to a new sustained release antibacterial agent, sulfaethylthiadiazole.

It is generally believed that environmental conditions outside hospitals are less conducive to the dissemination and perpetuation of antibiotic-resistant strains of all organisms, including the staphylococci. For this reason, the incidence outside hospitals can be expected to be smaller. However, some investigators^{1, 2} still feel that there is little evidence to refute the possibility of hospital-resistant strains of bacteria spreading to the community. Dowling,¹⁸ using the phage-typing technique, was able to show that penicillin-resistant strains of staphylococci contracted by hospitalized patients were spread to household contacts of the patients a few days after their return home. While this experiment did not follow the dissemination of resistant strains past household contacts, it would seem that the dissemination could continue *ad infinitum* depending on the number of contacts made by the non-hospitalized person. Just what part this method of dis-

TABLE 4
PENICILLIN-RESISTANT STRAINS OF
STAPHYLOCOCCUS FROM FOUR
GEOGRAPHIC COMMUNITIES

Community	No. Strains Tested	Sensitive	Resistant
Washington, D.C.	34	16	18
Malaya	21	20	1
Borneo	43	43	0
Mexico	14	14	0

seminating resistant strains of organisms plays in the overall incidence in the community is unknown.

In a community, the number of staphylococci resistant to a particular antibiotic seems to depend on the use of the antibiotic in that community. Hopps¹⁹ demonstrated this by determining the incidence of penicillin-resistant staphylococci in four communities in which penicillin had been used in different degrees (Table 4). Since the incidence of resistant organisms in hospitals also depends on the use or disuse of a particular antibiotic, it becomes apparent that previous exposure to antibiotics is important in the overall incidence of antibiotic resistance. In the United States where antibiotics are routinely used in nose drops, sprays, eye drops, ointments, and as food preservatives (usually in ineffective amounts), previous exposure to antibiotics may soon become an important factor in the overall incidence of antibiotic resistance in the community.

Based on the limited reports in the literature, it is difficult to estimate reliably the actual incidence of antibiotic-resistant staphylococci outside hospital communities. However, it seems that the trend toward an increased incidence has become established, and depends on such factors as the use or disuse of a particular antibiotic, pre-exposure to antibiotics, and the spread of organisms from hospital environs through hospital personnel and household contacts of hospitalized patients. If steps are taken in the community to minimize exposure to antibiotics and to control the appearance

and dissemination of drug-resistant organisms in the hospital, it is doubtful that the incidence of drug-resistant bacteria in the community will continue to grow.

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WOMAN'S AUXILIARY TO THE DELAWARE STATE MEDICAL SOCIETY

I am grateful to Mrs. Richard W. Comegys for enlightening us on the Kent County Auxiliary Activities, and to Mrs. J. Leland Fox for the recent Sussex County column. They were of extreme interest to me and served to stress clearly that it is the coordination and blending of all ideas and efforts that produces a well formulated, progressive program.

The term "Program" refers not only to the one planned for a particular meeting, but it also includes all we learn or do within the Auxiliary. The purpose is to inform, to create interest, and to develop points of view. The ultimate goal is to prepare our Membership for roles as informed leaders in health. Because of the broad scope in planning, and realizing the limitations and potentialities of each of our three County Auxiliaries, each must choose those topics which fit the needs and interest of their particular communities. For this reason, Medical Education Week — April 21st-27th — was observed by the Auxiliary being asked to tell the story of Progress in Medical Education to Women's groups within their communities. Several qualified speakers for other Women's organizations were provided and we feel that these groups now have a better understanding and appreciation of the achievements of our medical schools.

We must always remember that good programs don't just happen, but they are the result of good planning.

The thirty-fourth Annual Convention of the Woman's Auxiliary to the American Medical Association will be held in New York City — June 3d to 7th — with headquarters at the Hotel Roosevelt.

The tentative program schedule is as follows:

Saturday, June 1—Nominating and finance committee meetings.

Sunday, June 2—Registration (starting at noon) and meetings of the Board of Directors, and nominating, resolutions and revisions committees.

Monday, June 3—Round table discussions on legislation, public relations, program, organization, Today's Health, A.M.E.F., publications, with newsletters and Bulletin circulation. In the afternoon the annual tea in honor of the national president and president-elect will be held. Members and guests are cordially invited.

Tuesday, June 4—General meeting and luncheon in honor of the national past presidents. Dr. Howard Rusk, Director of the Institute of Physical Medicine and Rehabilitation of the New York University, Bellevue Medical Center, will be the guest speaker.

Wednesday, June 5—General meeting and luncheon in honor of the national president and president-elect. Dr. Dwight H. Murray, president of the American Medical Association, will be the guest speaker. Round table discussions on civil defense, mental health, recruitment and safety will be conducted in the afternoon immediately following luncheon.

The national parliamentarian, and the national chairman of finance, history, reference and revisions will be available for consultation and discussion of Auxiliary questions and problems.

Thursday, June 6—General meeting (until noon). Meeting of the Board of Directors will be held at one o'clock, followed by informal discussion of committee programs for 1957-58 with the committee chairmen.

Friday, June 7—Postconvention workshop of state presidents, presidents-elect and national committee chairmen.

This is your organization and has a relative value to you, therefore, I urge each of you to devote some part of your time to this meeting, especially the round table discussions. Your President will serve as a delegate, plus one delegate and one alternate for each one hundred members. Resolutions have been introduced to National, suggesting that the number of delegates from each state be lowered in an effort to gain a more efficient House of Delegates. The amendment, if passed, would read—"The voting delegates shall be the President of each Auxiliary and in addition one representative from each Auxiliary for each five hundred members or fraction thereof". Each State Auxiliary was asked to review this resolution and submit recommendations to the National Policy Committee.

A logical manner of approach was made—each of the three counties were contact-

ed and the amendment was unanimously approved.

The total potential delegation has seldom been reached, particularly if the convention city is too far distant from many states. For this reason, it is the hope that, with a lower number of wisely chosen, interested delegates, a greater efficiency will develop.

As a delegate to the annual convention, you assume a responsibility to your local, state and national auxiliaries. All members are invited to attend the sessions, but only voting delegates may introduce business or vote on the business of the convention. The Handbook will give the delegate a knowledge of procedures.

I look forward to the pleasure of seeing you at the Roosevelt.

NOTE

U.S. ARMY RESERVE HAS OPENINGS FOR DOCTORS, DENTISTS AND NURSES IN WILMINGTON

The 805th Station Hospital, the only U. S. Army Reserve medical unit in Wilmington has several openings for doctors, dentists and nurses. Commissions in the grades of First Lieutenant to Lieutenant Colonel in the case of doctors and dentists and from Second Lieutenant to Captain for nurses are available to both, veterans and non-veterans.

Regular weekly meetings of the 805th Station Hospital are held on Thursday evenings from 8 to 10 P.M. at the USAR Training Center at 11th and Washington Streets. During these meetings physical ex-

aminations of Reserve recruits are performed and the personnel is trained in all phases of hospital operation.

Each member of the unit receives a full day's pay based on his rank for each two-hour meeting attended. In addition, retirement benefits are acquired at the age of 60. Affiliation with an Army Reserve unit does not increase the likelihood of an involuntary call to active duty, except in the case of a national emergency to be declared by the President but does decrease any Reserve obligation.

Interested persons should call Lt. Col. K. Sachs, V.A. Hospital, Elsmere, Phone WYman 4-2511, Extension 303 (daytime) or WYman 4-0416 (evenings).

+ Guest Editorial +

MEDICAL WRITING CAN BE ENJOYABLE

Medical writing can be enjoyable! It may be difficult to start. It may be tedious to revise. But normally, the harder it is to write, the easier it is to read. Like the infant, the thoughts you put in writing can be as easy to conceive but hard to deliver. The pleasure is in the finished product. And even the process can be enjoyable!

Medical reading should be enjoyable! Within the mass of medical literature today, that which is difficult to read is doubly a wasted effort. I do not care to lose time interpreting an uninteresting report, nor do I always have the patience to revise and rewrite a pertinent observation which I feel should be published. Yet, you and I have the privilege as well as the obligation to both read and write about professional experiences.

I used to feel that a significant contribution to medical literature should include complete review of existing manuscripts, supplemented by toothy graphs, swirling statistics and numerous photographs. This is false. The most important element for a piece of medical writing is that the author "has something to write."

In many instances all that is needed can be in the form of a letter to an editor, stated in simple terms and ordinary language.

As physicians, we usually speak to our patients, colleagues and students. Yet, when

we change our communication medium to the written word we become artificial, use cumbersome phrases and tend to a stereotyped format. This is awkward and unnecessary! In addition, if you were to pad a bit of useful information, it would be as if the twinkling star were hidden behind a cloud. The most important means for the medical communication, then, is "brevity on a specific subject."

On the other hand, a gesture or inflection during conversation or in a lecture may have to be clarified, when writing, by use of precise terms, in order to avoid misinterpretation. Even our case histories, radiology and pathology reports, consultations, letters and narratives of operative procedure must be clear, concise and factual. Then they are easy to read and to understand.

Perhaps we should emphasize this more during all phases of medical school training and post-graduate education.

You and I can find enjoyment in medical writing. All we have to do is to understand what we write, and to state it clearly and concisely. Under such circumstances, our medical reading will also be enjoyable.

JULIAN A. STERLING

Reprinted from Philadelphia Medicine through courtesy of Dr. Sterling and the Editor.

THE HOME CARE PROGRAM PROGRESS REPORT

What has become known as the Home Care Program of the Delaware State Hospital, was started on February 15, 1956. Our experiences during this first year are of considerable interest to the medical profession in general. I would like to review briefly the purpose, the implications, and the results.

Since the introduction of Thorazine, in the beginning of 1954, drug treatments in psychiatry have brought about considerable changes in the management of psychiatric patients. The capacity of Thorazine and other drugs to modify psychopathological symptoms to the point of cure in some instances, and to a point of compensation in the majority of cases brought up the question of whether it would be possible to cut short hospital treatment. It seemed plausible that a certain group of patients could be restored to normal social activities if put on maintenance medication. Since diabetic and epileptic patients nowadays do well if placed on a maintenance level of medication, one is tempted to work out a similar mode of management for those patients whose symptoms can be suppressed by drugs, such as Thorazine and related phenothiazine compounds. The clinical, social and economic advantages of such an approach are obvious. With the support of a research grant the Home Care Program was organized in order to explore the potentialities of prolonged drug therapy. The following policies were implemented:

1. Patients selected for this program must have shown a favorable response to Thorazine or Compazine therapy in the hospital; they have not completely recovered, but are considered capable of making a good social and occupational adjustment provided medication will be continued.
2. The greater majority of these patients, admitted on commitment status, remain on trial visit while undergoing treatment; other patients, admitted on a voluntary basis, are discharged. These patients are equally eligible to receive the benefits of the program if they so desire.
3. The Program Supervisor, a graduate nurse from the staff of the Delaware State Hospital, dispenses medication, visits the patients at regular intervals in their homes, and reports to the medical staff about her observations.
4. Close contact is to be established with the family physician in order to explain the purpose of the treatment program. It should be stressed that the program pertains exclusively to psychiatric therapy and does not cover medical treatment in general. All patients are advised to consult their own physicians with regard to physical check-ups and treatment of non-psychiatric disorders.

Throughout this year patients were followed closely and seen at regular intervals at clinics held at the Delaware State Hospital. A total of 113 patients were treated; 99 received Thorazine, and 14 Compazine medication. While it is too early to report the results with Compazine, which was only recently added to this investigation, the Thorazine data can be presented briefly. Favorable responses were observed in 67 patients; 14 patients did not benefit and 18 had to be discontinued because of lack of cooperation with regard to medication schedules. The maximum daily dosages varied between 50 and 600 mg. per day. However, the average was 150 to 200 mg. per day. It should be stated that patients were not considered to respond favorably unless they resumed their pre-illness social and occupational activities.

Since this is merely a progress report and not a clinical evaluation, I shall not go into details of our findings. We hope that our clinical experiences with this therapeutic approach will be valuable in changing the present need for prolonged hospitalization.

I would like to express our gratitude to all physicians, whose cooperation contributed immensely to the success of this program.

F. A. Freyhan, M. D.

THE AMERICAN PHYSICIAN AND THE WORLD MEDICAL ASSOCIATION

The World Medical Association has become a strong factor in protecting and promoting the professional interests of the medical profession and the cause of world peace.

Now in its 10th year, The World Medical Association is a federation of the most representative national medical association in each of 53 nations. These member organizations represent more than 700,000 physicians. The American Medical Association is a leading member of The World Medical Association.

Doctors of medicine the world over cherish the same basic ideals of conduct and the same devotion to the welfare of mankind. The World Medical Association is cultivating the common purposes of the profession. This growing community of interest is a source of strength to the physicians of every land.

Already, by solid accomplishments, The World Medical Association has earned the right to call itself "the international voice of organized medicine". Thanks largely to the United States Committee and similarly supporting committees of physicians in other leading nations, The World Medical Association has a well-trying constitutional structure, a small but efficient secretariat, and a tri-lingual journal whose world-wide influence and value to the profession is rapidly growing. The permanent office of the secretariat — which serves both the association and the United States Committee — is located in the United States.

The membership of the United States Committee has been growing slowly but steadily. In 1955, the Committee reached its first important milestone of growth: a membership of 5,000 American physicians.

Even with this modest membership representing scarcely 3% of American medi-

cine, important achievements have been registered, many of which would have been impossible if the American pharmaceutical and related industries had not consistently matched the financial support given the United States Committee by its physician members.

In 1956, 128 members of the United States Committee attended the tenth General Assembly of The World Medical Association in Havana. This privilege is available to members of national supporting committees. There is unique inspiration, personal enjoyment and intellectual stimulus in meeting our colleagues from many lands, and in helping to formulate programs that may have incalculable benefits for the profession, and for the welfare of the world.

The World Medical Association assists traveling physicians by providing them with introductions to colleagues in other countries, by making speaking engagements for them abroad, by acquainting them with visiting doctors from other countries, and, of course, by sending the "World Medical Journal" to members of all national supporting committees.

In 1953, The World Medical Association sponsored the First World Conference on Medical Education, held in London. Representatives from many nations have reported concrete benefits from this epochal meeting in terms of better standards and practices in medical education in their countries. A Second World Conference on Medical Education is now being planned for 1959, to be held in the United States.

Two other World Medical Association accomplishments that have brought great credit to our profession and strengthened its solidarity throughout the world were the promulgation in 1948 of the Declaration of Geneva, comprising a modern re-state-

ment of the Hippocratic Oath, and the adoption in 1949 of an International Code of Medical Ethics.

The activities of The World Medical Association in the field of social security are of particular interest to American physicians. They have revealed boldly and unmistakably the physician's inherent and universal need for freedom from third-party interference with the practice of medicine. Such activities should not only fortify but inspire the efforts of American medicine to solve our socio-economic problems without resort to governmental subsidy or control.

On the International stage, The World Medical Association has endeavored to counter efforts of the International Social Security Association and the International Labour Organization to promote state medicine under social security programs. The World Medical Association has earned the respect of the International Labour Organization for its defense of the interests of medicine against the International Labour Organization Convention for Medical Socialization in 1952. Now The World Medical Association is attempting to wrest from the International Labour Organization the recognized world leadership in the field of occupational medicine.

The World Medical Association has engaged in efforts to protect medical research; to safeguard the National Pharmacopoeias and the rights of individuals discovering new drugs and agents to name them.

The World Medical Association has served the profession by representing it in relation

to the World Health Organization — the official health agency of the United Nations. In the attempt by various non-medical agencies to draft an International Code of Medical Law, The World Medical Association has insisted that such a code be based upon ethical principles acceptable to the profession.

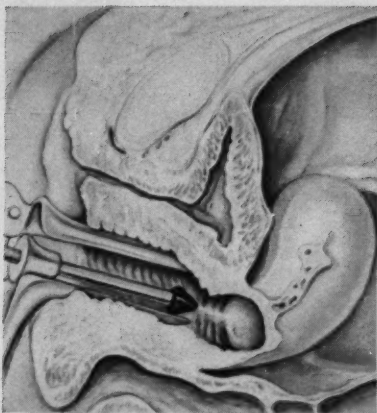
For all these activities, and for many more which demand our attention, additional funds are needed. Each new member not only contributes his nominal membership dues, but, more vitally, he lends his name and influence to the program of The World Medical Association and of its United States Committee.

America's world leadership challenges America's physicians to make the United States Committee a truly impressive and representative body of American physicians.

Every individual physician in the U. S. A. is eligible for membership in the United States Committee. Annual membership dues are \$10.00. The dues for Patron Members are \$100.00 or more. Many of our members regularly make contributions to the U. S. Committee, in addition to their annual dues. All such contributions to the United States Committee of The World Medical Association are tax deductible.

As the international voice of organized medicine, The World Medical Association is speaking for you. It is seeking to promote and protect your interests. You are urgently invited to help these efforts along, by joining the United States Committee, and participating in its work.

COMPREHENSIVE VAGINITIS REGIMEN



Powder Insufflation



Tablet Insertion

Floraquin® Rebuilds the Defense Mechanism in Vaginitis

Combined office and home treatment with Floraquin provides a comprehensive regimen which encourages restoration of the normal "acid barrier" to pathogenic infection.

Vaginal secretions normally show a high degree of protective acidity (pH 3.8 to 4.4). When this "acid barrier" is disturbed, growth of benign Döderlein bacilli is inhibited and that of pathogens encouraged. Floraquin not only provides an effective protozoacide and fungicide (Diodoquin®) destructive to pathogenic trichomonads and yeast, but also furnishes sugar and boric acid for reestablishment of the normal vaginal acidity and regrowth of the normal protective flora.

Suggested Office Floraquin Insufflation

"... the vagina is treated daily by swabbing with green soap and water, drying and insufflation of Floraquin powder."*

Suggested Home Floraquin Treatment

"The patient is also issued a prescription for Floraquin vaginal suppositories which she is instructed to insert high into the vagina each evening. On the morning following each application of these suppositories, the patient should take a vinegar water douche. . . ."

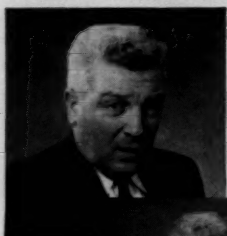
A Floraquin applicator is supplied with each box of 50 Floraquin tablets. G.D. Searle & Co., Chicago 80, Illinois, Research in the Service of Medicine.

*Williamson, P.: Trichomonad Infestation, M. Times 84:929 (Sept.) 1956.

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Riker brand of isoproterenol HCl 0.25% solution in inert, nontoxic aerosol vehicle. Each ejection delivers 0.06 mg. isoproterenol. In 10 cc. vial with metered-dose valve. • Indicated in acute or recurring bronchospasm.

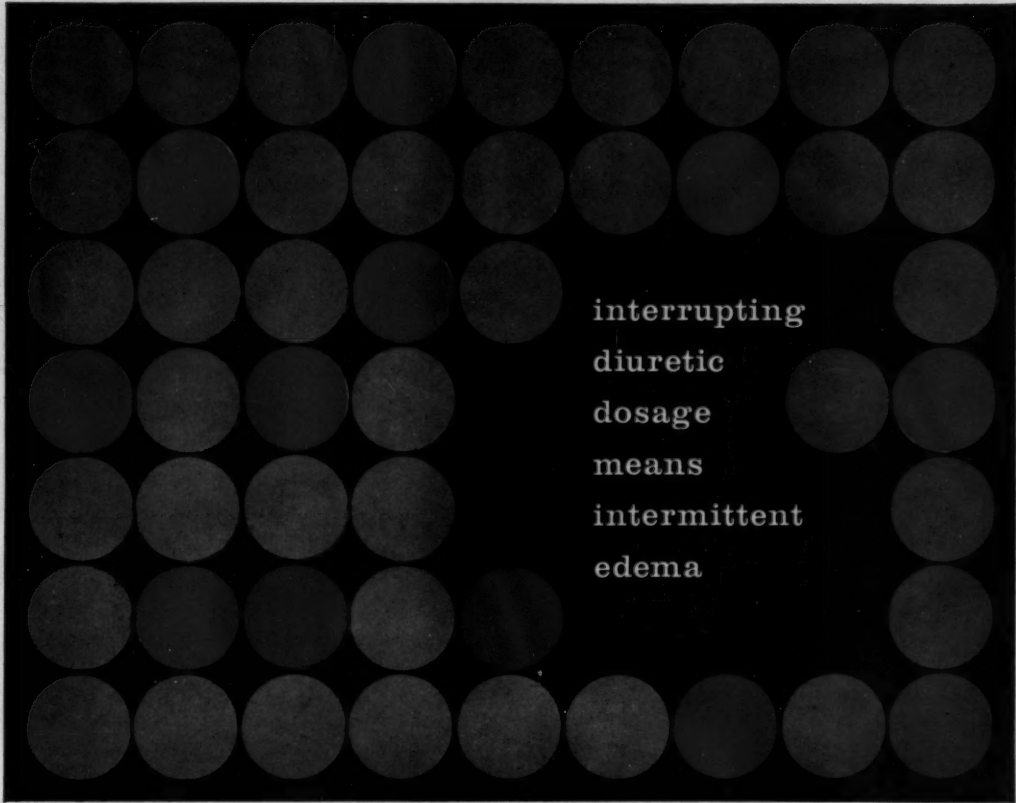
Note: First prescription should include desired medication and Medihaler Oral Adapter, supplied with pocket-sized plastic container.

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is also available in Medihaler-Nitro™ (octyl nitrite) for the rapid relief of angina pectoris...and Medihaler-Phen™ (phenylephrine-hydrocortisone-neomycin) for lasting, effective relief of nasal congestion.



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dosage
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PATIENTS IN FAILURE NEED AN ORGANOMERCURIAL

Diuretics needing "rest periods," whether enforced by dosage restriction to once daily, or by omission to alternate days, inevitably fail to achieve sustained control of edema.

The organomercurials never require interruption of dosage to prevent refractoriness and can maintain patients continuously in the edema-free state.

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In Feeding Prematures

Recent metabolic studies have established rational feeding procedures for prematures.

The initial feeding, 12 hours after birth, consists of one dram of 5 per cent dextrose. This solution is increased by one dram at 2-hour intervals if tolerated and retained.

After twenty-four hours, breast milk or formula (table below) gradually replaces the prelacteal feeding at 2-hour intervals. The volume of a feeding may be increased up to 2 drams daily until maintenance caloric requirements are fulfilled by the fifth day. If the infant shows signs of intolerance, the formula increase is made more slowly and the fluid requirement fulfilled parenterally.

Successful feeding mixtures consist of dilutions of powdered half-skimmed or evapor-

ated whole cow's milk, skimmed or whole lactic acid milk. These formulas contain high protein, moderate carbohydrate and low fat, yielding about 120 calories and 150 cc. fluid per kgm. body weight.

The problems of prematures are always the same but the solutions differ with each era. Today the moderate carbohydrate requirement for normal infants as well as prematures is fulfilled by KARO® Syrup as adequately as a generation ago. Whatever the type of milk adapted to the infant, KARO may be added confidently because it is a balanced mixture of lower sugars resistant to fermentation, non-laxative, easily assimilated and well tolerated by all infants.

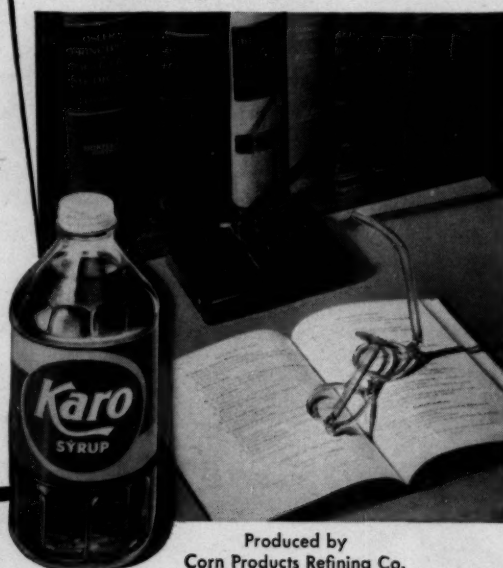
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R_x FIRST FORMULAS FOR PREMATURES	
Fresh or whole lactic acid milk	6 oz.
Water	12 oz.
KARO	1 oz.
Evaporated milk	3 oz.
Water	15 oz.
KARO	1 oz.
Dried milk (half-skimmed)	4 tbsp.
Water	18 oz.
KARO	1 oz.

Feedings: 1½ oz. x 12 x 2 hours
Measures: 1 oz. KARO = 2 tablespoons
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Equivalents: Red Label KARO or Blue Label KARO may be used interchangeably in all formulas.

Adapted from Nelson's Pediatrics, Saunders, Phila. 1954



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designed to **control anxiety**
in Arthritis, Asthma, Allergic Dermatoses
with **lower corticoid dosage**

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provides the emotional tranquilizer, ATARAX® (hydroxyzine) and the preferred corticoid, STERANE® (prednisolone) • control of emotional factors by tranquilization enhances response to the corticoid for greater clinical improvement • often permits substantial reductions in corticoid dosage, accompanied by reduction of hormonal side effects • confirmed by marked success in 95% of 1095 cases of varied corticoid indications¹

ATARAXOID now written as

Ataraxoid 5.0

5 mg. prednisolone, 10 mg. hydroxyzine hydrochloride, in green, scored tablets. Bottles of 30 and 100.

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Ataraxoid 1.0

1.0 mg. prednisolone, 10 mg. hydroxyzine hydrochloride, in orchid, scored tablets. Bottles of 100.

advantages: (1) greater flexibility of dosage
(2) effective tranquilization permits lower corticoid dosage

formerly **Ataraxoid**
NOW written **Ataraxoid 5.0**

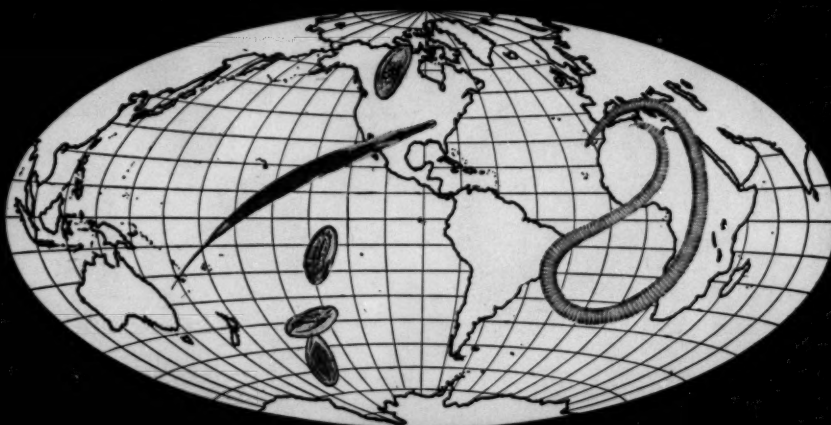
¹ Personal communications

*Trademark

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relaxes
both mind
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*for anxiety
and tension in
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- nonaddictive, relatively nontoxic, well tolerated
- well suited for prolonged therapy
- no blood dyscrasias, liver toxicity, Parkinson-like syndrome or nasal stuffiness
- chemically unrelated to phenothiazine compounds and rauwolfia derivatives
- orally effective within 30 minutes for a period of 6 hours

For treatment of **anxiety and tension states and muscle spasm**

Miltown®

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Tranquilizer with muscle-relaxant action



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SUPPLIED: 400 mg. scored tablets (Bottles of 50 tablets)
Usual Dosage: 1 or 2 tablets i.i.d.

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nonaddictive
relatively nontoxic
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For Anxiety
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Practice

1 "Habituation does not follow the use of Miltown and . . . withdrawal symptoms have been completely absent."

Pennington, V.M.: J.A.M.A. In press, 1957.

2 "We found meprobamate ['Miltown'] to be a drug of extremely low toxicity and well tolerated . . . no tendency to addiction was encountered."

Altschul, A. and Billow, B.: New York State J. Med. In press, 1957.

3 "No patient developed a tolerance to the drug, although medication was prolonged in some cases as long as six months."

Gillette, H. E.: Internat. Rec. Med. 169: 453, 1956.

4 "Complications associated with long-term therapy are probably seen in lowest incidence with meprobamate ['Miltown']. "

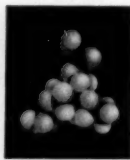
Fazekas, J. F., Shea, J. G. and Sullivan, P. D.: GP 14: 75, 1956.

5 "Thus far, there has been very little evidence of actual habituation to meprobamate ['Miltown']. No real tolerance has been observed."

Borrus, J. C.: Med. Clinics of North America. In press, 1957.

THE ORIGINAL MEPROBAMATE®
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THE MILTOWN®
MEPROBAMATE MOLECULE

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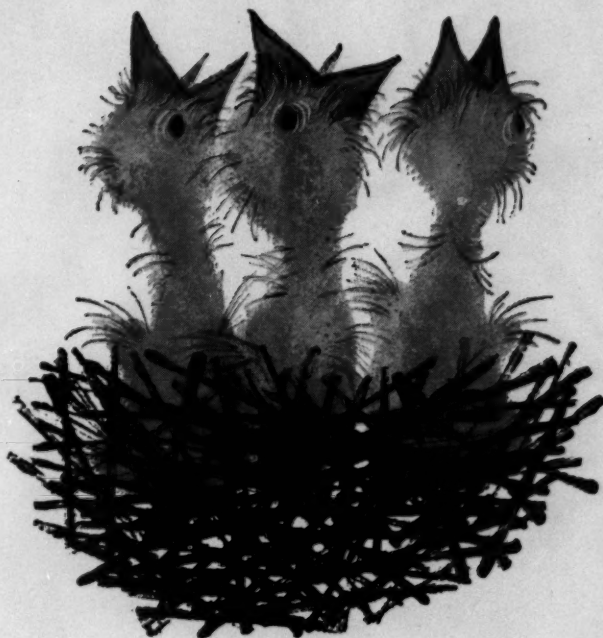
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children are often this eager...

Because Rubraton tastes so good, most children actually look forward to taking it. What better way could there be for providing these essential nutrients?

Rubraton is indicated for combatting many common anemias and for correcting mild B complex deficiency states. It may also prove useful for promoting growth and stimulating appetite in poorly nourished children. (Not intended for treatment of pernicious anemia.)

Dosage: 1 or 2 teaspoonfuls t.i.d.

Supply: Bottles of 8 ounces and 1 pint.

1 teaspoonful (5 cc.) supplies:

Elemental Iron	38 mg.
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Thiamine mononitrate	1.0 mg.
Riboflavin	1.0 mg.
Niacinamide	5 mg.
Pantothenic acid (Panthenol)	1.5 mg.
Pyridoxine hydrochloride	0.5 mg.

Alcohol content: 12 per cent

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SQUIBB IRON, B COMPLEX AND B₁₂ VITAMINS ELIXIR

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**WHENEVER
COUGH THERAPY
IS INDICATED**

Hycodan[®]

(Dihydrocodeinone with Homatropine Methylbromide)

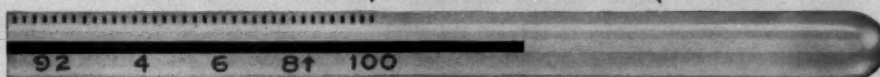
- Relieves cough quickly and thoroughly
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- And pleasant to take

Syrup and oral tablets. Each teaspoonful or tablet of Hycodan[®] contains 5 mg. dihydrocodeinone bitartrate and 1.5 mg. Mesopin.[†] Average adult dose: One teaspoonful or tablet after meals and at bedtime. May be habit-forming. Available on your prescription.

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can you read this thermometer,



doctor?

Naturally not. Missing calibration makes it worthless.

Equally useless and dangerous is a "quantitative" urine-sugar test that does not quantitate dependably, or omits readings in the critical range.

Enzyme urine-sugar tests are sensitive and specific for glucose—excellent "yes" or "no" tests but undependable for quantitation. King and Hainline,¹ after testing 1,000 urines, found an enzymatic urine-sugar test unable to distinguish in the important range between $\frac{1}{2}$ per cent and 2 per cent or more of urinary glucose. Leonards,² in a report on 4,020 tests, revealed that "...in 502 out of 804 tests the wrong interpretation was made." He concluded that enzymatic urine-sugar testing "...as a quantitative procedure is unsatisfactory and can lead to serious error in the interpretation of a patient's clinical condition."²

Failure to recognize this limitation of enzyme tests may result in incorrect insulin dosage,² and may lead to diabetic complications.

(1) King, J. W., and Hainline, A., Jr.: Commercial Glucose Oxidase Preparations for the Detection of Glucose in Urine, *Cleveland Clin. Quart.* 23:212, 1956. (2) Leonards, J. R.: Evaluation of Enzyme Tests for Urinary Glucose, *J.A.M.A.* 163:260 (Jan. 26) 1957.

reliable readings throughout the critical range—
does not omit $\frac{3}{4}\%$ (++) and 1% (++++)

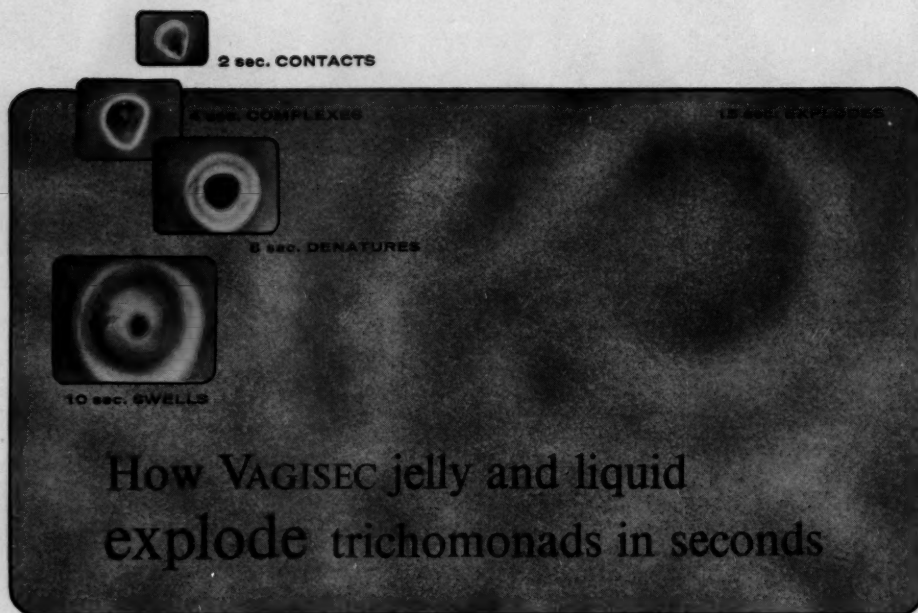
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CLINITEST®
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a 15 year "standard" in urine-sugar testing



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38187



VAGINAL trichomoniasis quickly yields to VAGISEC® liquid and jelly.¹⁻⁵ These unique trichomonocides *explode* flagellates after 15 seconds' contact. Following a VAGISEC douche, VAGISEC jelly maintains trichomonocidal effectiveness 'round-the-clock. With this new approach, therapy succeeds in more than 90 per cent of cases.⁴

Research proves effectiveness—In hundreds of tests with slide preparations, mixtures of VAGISEC jelly and vigorous cultures of *Trichomonas vaginalis* have been examined under a phase-contrast microscope.^{3,6} The trichomonads *explode and disperse within 15 seconds* after contact with jelly—exactly like those in a VAGISEC douche solution.³⁻⁶

Explosion succeeds—VAGISEC liquid and jelly penetrate rapidly to trichomonads covered by vaginal mucus and cellular debris and *explode* them, avoiding post-treatment flare-ups.³⁻⁵ VAGISEC therapy often rids stubborn clinical cases of "trich" even after other agents fail.

Why parasites explode—A wetting agent, a detergent and a chelating agent, combined in balanced blend in VAGISEC liquid and jelly,³⁻⁵ act to weaken the parasites' cell membranes, remove waxes and lipids, and denature the protein. Then the trichomonads imbibe water, swell and explode into fragments . . . all within 15 seconds.

The Davis technique†—Dr. Carl Henry Davis, co-discoverer of VAGISEC, recommends a combination of office treatments with VAGISEC

liquid and 'round-the-clock home therapy with the liquid and jelly.³ This regimen halts vaginal trichomonal infections and ensures *continuous* control until all trichomonads are gone. For a small percentage of women who have an involvement of cervical, vestibular or urethral glands, other treatment will be required.^{1,3-5}

Re-infections can and do occur from the husband^{2-5,7,8}—Prescribing RAMSES®, high quality prophylactics, as protection against conjugal contagion ensures husband cooperation. Most of them know and prefer RAMSES—the one with "built-in" sensitivity. RAMSES are superior, transparent rubber prophylactics, naturally smooth, very thin, yet strong. At all pharmacies.

Active ingredients in VAGISEC liquid: Polyoxyethylene nonyl phenol, Sodium ethylene diamine tetra-acetate, Sodium dioctyl sulfosuccinate. In addition, VAGISEC jelly contains Boric acid, Alcohol 5% by weight.

References: 1. Decker, A., and Decker, W. H.: Practical Office Gynecology, Philadelphia, F. A. Davis Company, 1956. 2. McGoogan, L. S.: J. Michigan M. Soc. 55:682 (June) 1956. 3. Davis, C. H. (Ed.): Gynecology and Obstetrics (revision), Hagerstown, W. F. Prior, 1955, vol. 3, chap. 7, pp. 23-33. 4. Davis, C. H.: West. J. Surg. 63:53 (Feb.) 1955. 5. Davis, C. H.: J.A.M.A. 157:126 (Jan. 8) 1955. 6. Molomut, N., Port Washington, N. Y.: Personal communication (Jan.) 1957. 7. Draper, J. W.: Internat. Rec. Med. 168:563 (Sept.) 1957. 8. Feo, L. G., et al.: J. Urol. 75:711 (Apr.) 1956.

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In the nonhormonal treatment of arthritis¹
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broad scope of usefulness,
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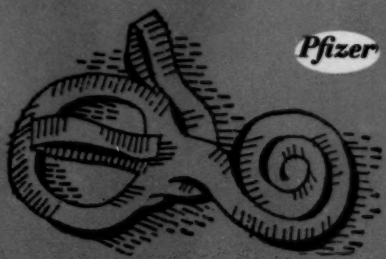
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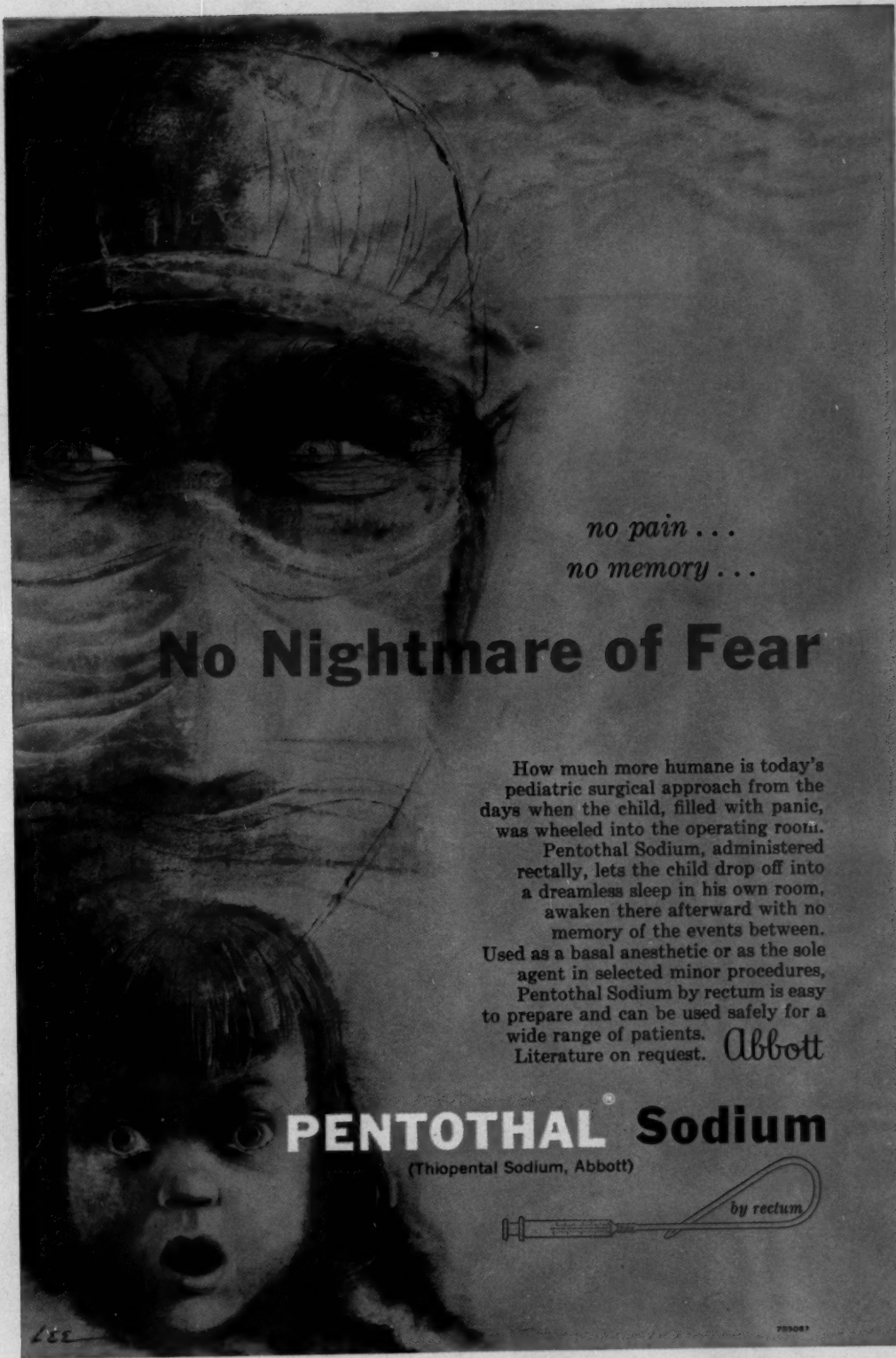
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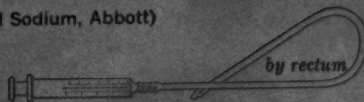
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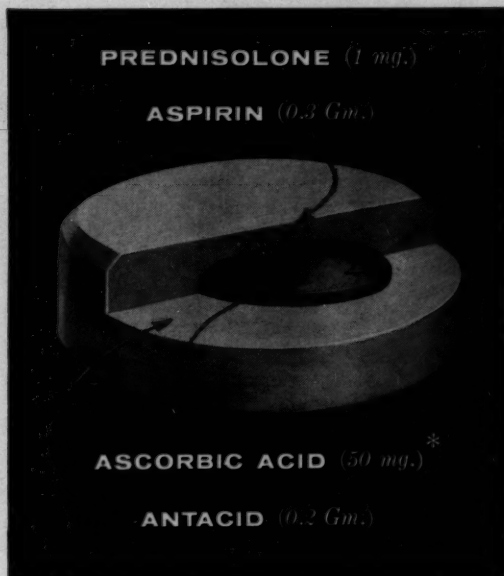
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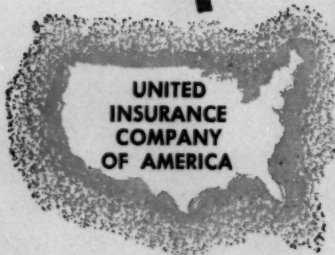
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1. Knoch, H.R., and Kirk, R.: Prochlorperazine—A New Agent for the Treatment of Psychic Stress, in manuscript.

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